

## Original Article

# Glucose Pump Test can be Used to Measure Blood Flow Rate of Native Arteriovenous Fistula in Chronic Hemodialysis

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### ABSTRACT

**Purpose:** In chronic hemodialysis patients, the low flow of vascular access may leads to inadequate dialysis, increased rate of hospitalization, morbidity, and mortality. It was found that surveillance should be performed for native arteriovenous (AV) should not be performed for AV graft in various studies. However, surveillance was done in graft AV fistulas in most studies. Doppler ultrasonography (US) was suggested for surveillance of AV fistulas by the last vascular access guideline of National Kidney Foundation Disease Outcomes Quality Initiative (NKF KDOQI). The aim of study is to determine whether glucose pump test (GPT) is used for surveillance of native AV fistulas by using Doppler US as reference. **Methods:** In 93 chronic hemodialysis patients with native AV fistula, blood flow rates were measured by Doppler US and GPT. For GPT, glucose was infused to 16 mL/min by pump and was measured at basal before the infusion and 11 s after the start of the infusion by glucometer. Doppler US was done by an expert radiologist. Used statistical tests were Mann-Whitney *U* test, Friedman test, regression analysis, and multiple regression analysis. **Results:** Median values of blood flow rates measured by GPT (707 mL/min) and by Doppler US (700 mL/min) were not different ( $Z = 0.414$ ,  $P = 0.678$ ). Results of GPT and Doppler US measurements were positive correlate by regression analysis. The mean GPT value of diabetic patients ( $n = 39$ ; 908 mL/min) was similar to that of nondiabetic patients ( $n = 54$ ; 751 mL/min;  $Z = 1.31$ ,  $P = 0.188$ ). GPT values measured at three different dialysis session did not differ from each other that by Friedman test ( $F = 0.92$ ,  $P = 0.39$ ). This showed that GPT was stable and reliable. **Conclusions:** Glucose pump test can be used to measure blood flow rate of native AV fistula. GPT is an accurate and reliable test.

**KEYWORDS:** *Glucose pump test, Native arteriovenous fistula, Hemodialysis, Blood flow rate*

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## INTRODUCTION

In chronic hemodialysis patients, vascular access patency is significant for optimal management. Low access blood flow rates and reduction of patency can cause inadequate hemodialysis; thus, morbidity and mortality can be increased.<sup>[1]</sup> Asymptomatic but hemodynamically significant stenosis is detected by surveillance program.

Surveillance is the periodic evaluation of the vascular access by using tests and physical examination.<sup>[2]</sup> Routine surveillance for graft arteriovenous (AV) stenosis cannot be recommended

for reduction of graft thrombosis.<sup>[3,4]</sup> In 69 full articles, and 12 randomized controlled trials, it was reported that surveillance of AV graft has not recommended, but native AV fistula should be monitored.<sup>[5,6]</sup> It was reported that physical examination of access, direct flow measurements, and Doppler ultrasound (US) should be preferred for surveillance of AV fistula according to

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clinical practice guideline for vascular access of NKF KDOQI.<sup>[7]</sup> An access flow rate should not be less than 600 mL/min for grafts and less than 400 mL/min for native AV fistula.<sup>[7]</sup> That is, normal blood flow rates are different between grafts and fistulae. Glucose pump test (GPT) was mostly done in patients with AV graft in other studies. Doppler US is expensive and time consuming, and requires specialist. However, GPT is cheap and can be done at the bedside in hemodialysis session.<sup>[8-11]</sup>

The aim of study is to investigate whether GPT can be used to determine blood flow rates of native AV fistulas by using Doppler US as reference.

## PATIENTS AND METHODS

Ninety-three chronic hemodialysis patients (male: 45, female: 48) with native AV fistula were included to this study. Mean age of the patients were  $50.8 \pm 17.1$  years.

Informed consent was obtained from all of the patients for medical procedures. This article is compatible with the ethic guidelines for human studies. Study protocol of the article has been approved by the local ethic committee on human research.

Laboratory results of the patients were obtained from medical files. Arterial blood pressure from nonvascular access arm was measured by aneroid sphygmomanometer.

The patients did not suffer from heart failure, edema, or calcified vascular access. Calcified vascular access was detected by x-ray. Etiologies of chronic kidney disease were idiopathic in 36 (38.7%) patients, diabetes mellitus in 27 (29%) patients, hypertension in seven (7.5%) patients, autosomal dominant polycystic kidney disease in four (4.3%) patients, pyelonephritis in four (4.3%) patients, glomerulonephritis in three (3.2%) patients, familial mediterranean fever in two (2.2%), and other causes in 10 (10.8%) patients. AV fistulas were brachial in 70.3% patients and radial in 29.7% patients. Patient characteristics are shown in [Table 1].

## GLUCOSE PUMP TEST

GPT process requires a constant glucose infusion, by a syringe pump, into the arterial line and two blood withdrawals from the venous needle, one basal before the infusion and the other 11 s after the start of the infusion.

Before the start of hemodialysis, the arterial needle was placed, and connected it to an infusion pump (Plussep 12 S). Syringe with 50 mL was filled with 10% glucose solution and infusion rate was adjusted to 16 mL/min. Shortly before infusion, basal blood sample (0.2mL) was drawn from venous needle; then glucose infusion was started and a second blood sample was drawn from venous line after 11 s. Glucose levels were measured in

all patients by using same glucometer (Accu-check) and glucose measurement strips (Accu-check go). Based on the glysemic values, flow rate of fistula was calculated with the equation below.<sup>[8,9]</sup>

$$Q_a = Q_i (C_i - C_2) / (C_2 - C_1)$$

$Q_a$  is flow rate of native fistula (mL/min);  $Q_i$ , infusion rate (mL/min);  $C_i$ , concentration of glucose infused (mg/dL);  $C_1$ , preinfusion glysemic level (mg/dL); and  $C_2$ , postinfusion glysemic level (mg/dL).

GPT was done to investigate the reliability of the test at the start of the three consecutive dialysis (GPT1, GPT2, GPT3), and mean of GPT values were calculated.

Arteriovenous fistula (AVF) needle gauge was 16-G needle distance was 5-15 cm: puncture type-always same region and same person puncturing.

## DOPPLER ULTRASONOGRAPHY

The blood flow rates of native AV fistulas were measured by using color Doppler US (General Electric) everyday, between the two dialysis. It was evaluated by the same expert radiologist in the longitudinal and transverse planes from the arterial anastomosis through the entire access. Doppler US was accepted as reference for blood flow rate measurement of native AV fistula. Doppler US was performed one time. Three measurements were made and average of three measurements taken.

Doppler US examination of the AVF was performed with the patient in an upright seated position. The arm was positioned at 45° from the body and comfortably supported by towels on a mobile instrument stand. Standard angle was 60°, corrected whenever possible with changes in transducer position. Next, vessel diameter value was measured after image freezing, and flow volume measure was then calculated using the device software. Final value used in the study was the arithmetic mean of three measurements, both of diameter and flow. It is used to calculate blood volume flow. Blood volume flow is calculated by equipment software, using the following formula:

Volume (mL/min): Cross-sectional area (cm<sup>2</sup>) × Mean velocity (cm/s) × 60

Cross-sectional area (cm<sup>2</sup>):  $\pi d^2/4$

(d: diameter )

## Statistical analysis

D'Agostino-Pearson test, Mann-Whitney  $U$  test, correlation test, regression test, multiple regression test, Friedman test were used for statistical analysis. Friedman test is a nonparametric statistical test. Friedman test was used because GPT were made at different times. Similar

to the parametric repeated measures ANOVA, it is used to detect differences in treatments across multiple test attempts.  $P < 0.05$  used for "significance".

## RESULTS

Blood flow rates of native AV fistula were measured by Doppler US and GPT [Table 2].

GPT1, GPT2, and GPT3 were measurements, that is made for the same patient at three different times. These measurements were grouped as GPT1, GPT2, GPT3 and were evaluated by Friedman test. There was no difference among groups ( $F = 0.928, P = 0.397$ ).

Arithmetic mean of sum of the GPT1, GPT2, and GPT3 were calculated as mean GPT. GPT1, GPT2, GPT3 and mean of GPT were compared. They were not found as different ( $F = 0.576, P = 0.631$ ).

Values of Doppler US, GPT1, GPT2, GPT3 and mean GPT groups were compared with Friedman test. It was not found difference among values ( $F = 0.455, P = 0.769$ ).

Blood flow rates of native AV fistula, measured by Doppler US and GPT (mean) were compared with Mann-Whitney  $U$  test. It was found that they are not different ( $Z = 0.414, P = 0.678$ ).

Doppler US and GPT measurements were found as similar by regression analysis ( $R^2 = 0.239, P < 0.001$ ).

We found a significant positive correlation between GPT and Doppler US ( $r = 0.49, P < 0.001$ ).

Effects of blood glucose levels before dialysis session on GPT measurements was analyzed by correlation test. It was not found significant correlation between blood glucose levels and GPT1, GPT2, GPT3 (respectively,  $r = 0.044, P = 0.668; r = 0.097, P = 0.35; r = 0.065, P = 0.533$ ). Thus, it was established that blood glucose levels did not affect to GPT measurements.

Mean of GPT was  $751.94 \pm 377.90$  in nondiabetic patients ( $n = 54$ ) and  $908.53 \pm 508.33$  in diabetic patients ( $n = 39$ ). There was no significant difference for GPT between groups ( $Z = 1.31, P = 0.188$ ). That is, GPT can be also used for diabetic patients.

Blood flow rates of AV fistula can be affected by osmotic and oncotic pressures of blood and arterial blood pressures. Sodium, glucose, hemoglobin, and albumin are significant effectors, created osmotic and oncotic pressures [Table 3]. Blood levels of hemoglobin (Hb), albumin, sodium (Na), and glucose were evaluated by multiple regression analysis method, whether it was be correlation between this values and flow rates, determined by Doppler US and GPT. It was determined

that flow rates, measured by Doppler US were not affected by Hb ( $P = 0.652$ ), albumin ( $P = 0.838$ ), sodium ( $P = 0.124$ ), and glucose ( $P = 0.904$ ) levels ( $R^2 = 0.0331$ ). Similarly, mean flow rates, measured by GPT were not affected by Hb ( $P = 0.462$ ), albumin ( $P = 0.471$ ), sodium ( $P = 0.376$ ), and glucose ( $P = 0.686$ ) levels ( $R^2 = 0.0259$ ).

Insufficient AV fistula flow rate can leads to dialysis failure. One of the indicators of dialysis failure is urea kinetic modeling (Kt/V). It was not found significant correlation between Kt/V values and blood flow rates that are measured by both GPT and Doppler US (respectively,  $r = 0.173, P = 0.095; r = -0.04, P = 0.689$ ). That is, correlation between AV fistula flow rates and adequacy of dialysis can be not found. All patients was divided to two groups as patients with low Kt/V ( $< 1.2$ ) ( $n = 10$ ) and normal Kt/V ( $n = 83$ ). In these groups, vascular flow rates, measured by Doppler US and GPT were compared by using Mann-Whitney  $U$  test. The AV fistula blood flow rates were not different in the patients with low Kt/V and with normal Kt/V [Table 4].

Effects on native AV fistula flow rates of arterial blood pressures were investigated by multiple regression analysis. It was found that systolic ( $P = 0.660$ ) and diastolic ( $P = 0.903$ ) blood pressures did not affect to flow rates, measured by Doppler US ( $R^2 = 0.0103$ ). Similarly, systolic ( $P = 0.733$ ) and diastolic ( $P = 0.839$ ) pressures did not affect to flow rates, measured by GPT ( $R^2 = 0.0101$ ).

**Table 1: Patient characteristics**

Gender	45 male, 48 female
Age (years)	50,8 ± 17,1
Duration(hemodialysis)(month)	50,1 ± 27
Kt/V	1,51 ± 0,29
Vascular access	66 brachial (70,3%), 27 radial (29,7%)
SBP	129 ± 22,7 mmHg
DBP	75,9 ± 12,2 mmHg
MAP	93,3 ± 14,4 mmHg

SBP: systolic blood pressure, DBP: Diastolic blood pressure, MAP: mean arterial pressure.

**Table 2: Vascular access flow rates (ml/min)**

Lowest	Highest	Mean±SD	Median
GPT1	296	2388	823.16±459.85
GPT2	288	2816	832.55±501.27
GPT3	294	2569	826.47±484.24
GPT mean	297	2373	826.43±435.25
Doppler US	240	2370	809.87±444.38

ml.: mililiters, min.: minutes

**Table 3: Parameters, affecting to vascular access flow rate in the patients.**

	Lowest	Highest	Mean±SD	Median
Glucose(mg/dL)	64	415	121.34±64.79	97
Hemoglobin(g/dL)	6.2	15.1	10.5±1.53	10.5
Albumin(g/dL)	2.7	4.7	3.92±0.40	4.0
Sodium(mEq/L)	127	144	135.7±3.61	136
Kt/V	0.87	2.15	1.51±0.29	1.50
Systolic BP(mmHg)	80	170	129.46±22.18	130
Diastolic BP(mmHg)	40	100	75.91±12.26	80

SD:Standart Deviation, BP:Blood pressure

**Table 4: The comparison of flow rates based on Kt/V values**

	Low Kt/V	Normal Kt/V	Z	p
Doppler US(mL./min.)	954±607	793±422	0.850	0.395
GPT(mL/min.)	745±186	836±456	0.086	0.930

## DISCUSSION

A functional vascular access is critical importance for the prognosis of hemodialysis patient. Loss of patency of the vascular access limits hemodialysis process and may result in under dialysis that leads to increased morbidity and mortality.<sup>[12,13]</sup>

Surveillance of AV access for hemodialysis prevents access thrombosis and improves the quality of care.<sup>[14]</sup> The most common screening tests are access blood flow rate and dialysis venous pressure measurements.<sup>[15,16]</sup>

Access flow can be measured Doppler US and MR angiography (direct methods) or US dilution, transcutaneous Access flow rate, glucose infusion, differential conductivity, and ionic dialysance (indirect methods).

In our study, we compared GPT with Doppler US that most frequently used method of access flow rate.

There are numerous studies comparing with access flow rate measurements.

Variable pump flow based Doppler US method is found a noninvasive, accurate, and reliable procedure for vascular access flow measurement in HD patients. Doppler US method is correlated with ultrasound dilution (UD) method.<sup>[17]</sup>

In a study with 33 hemodialysis (HD) patients, there are 25 synthetic grafts and eight autogenous AV fistulae. Access blood flow measurements were done by ultrasound dilution (UD) and GPT during hemodialysis. There was a strong linear correlation between the two methods ( $P < 0.001$ ). However, number of the patients with autogenous AV fistula were low.<sup>[10]</sup>

In 30 chronic HD patients with AV graft, GPT was compared with UD test. It was shown that GPT is an accurate, quick, and economic test for blood flow monitoring.<sup>[11]</sup>

In 27 chronic HD patients, blood flow rates were measured by Doppler US, GPT, and UD test. Mean values of GPT and Doppler US were agreement ( $P = NS$ ). Similarly, it was determined a good correlation between GPT and UD results by the regression analysis.<sup>[9]</sup>

To measure access blood flow, GPT was compared with the urea test. It was determined a good correlation between the two methods. The GPT is reported as a reliable technique for measuring blood flow in vascular accesses.<sup>[3]</sup>

Fifty-nine hemodialysis patients with native AV fistulae were evaluated by UD technique, Doppler US, and fistulography. Both ultrasound techniques predicted access stenosis ( $P < 0.01$ ). Performance was found similar between both techniques. It was reported that blood flow monitoring of AV access by ultrasound provided a reasonable prediction of access stenosis.<sup>[18]</sup>

In our study, number of the patients ( $n = 93$ ) with native AVF was much higher than other studies. GPT and Doppler US method were compared. Results of two methods were found similarly. GPT-even in one-time measurement-correlated with ultrasound but we have made three measurements. We calculate the average of three measurements. Consequently, GPT can be advisable for surveillance of native AV hemodialysis access. GPT is cheap, easy, and does not require expert.

In our study, it may be considered objectionable infusion of glucose in diabetic patients, but we've infused only %10 glucose 2.93 mL.

## CONCLUSION

Finally, native AV fistula flow rates, measured by GPT were found similar to flow rates, measured by Doppler US. Measurement with GPT is found stable and reliable. Thus, utilization of GPT can be recommended to measure blood flow rates of native AV fistula.

## COMPLIANCE WITH ETHICAL STANDARDS

*Funding:* This study was not funded.

*Conflict of interest :* Yasemin Coskun declares that she has no conflict of interest. Nedim Yilmaz Selcuk declares that he has no conflict of interest. Lutfullah Altintepe declares that he has no conflict of interest. Ibrahim Guney declares that he has no conflict of interest.

*Ethical approval :* All procedures performed in studies involving human participants were in accordance with



the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

*Informed consent* : Informed consent was obtained from all individual participants included in the study.

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Nil

### Conflict of Interest

There are no conflicts of interest

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